Retrospective evaluation of BMP (Bone Morphogenetic Protein) as an osteoinductor factor in complex fractures.

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INTRODUCTION

Since the discovery of bone morphogenetic proteins (BMP), it has come a long way in its identification and applications in traumatology. These are potent growth factors of the TGF-β superfamily synthesized primarily by osteoblasts. Currently there are more than 20 subtypes, among which BMP-2 stands out for its high osteoinductive capacity. With the advancement of molecular techniques it has been possible to purify human recombinant BMP 2 (rhBMP-2), a substance that simulates BMPs, and is marketed as TruScient® in order to stimulate bone consolidation in cases with delayed bone healing or non-unions.

STUDY AIMS

The purpose of this study is to verify the efficacy of TruScient® in healing and bone formation by analyzing different complicated orthopedic cases from the Hospital Clínic Veterinari of the UAB in which it was used.

MATERIALS & METHODS

Individual details of the 13 clinical cases that were part of the study are displayed in **Table 1**.

Table 1. *Details of the clinical cases used in the study.*

Case	Species	Breed	Age	Sex	Weight (Kg)	Surgery reason	Surgical treatment	BMP extremity	Evolution	Complications	Consolidation time (months)
1	Feline	European Shorthair	2 years	F	3,5	Femoral fx	Osteosynthesis plate, 7 screws, 2 cerclages and BMP.	RPE	Favorable	Yes[1,2]	2
2	Canine	Miniature Pinscher	8 months	M	5,14	Bilateral fx of ulna/radius	Osteosynthesis plate, 6 screws and BMP.	RAE	Favorable	No	1,5
3	Feline	European Shorthair	1 year	CM	4,5	Humerus fx	Tie-in, 3 cerclages, 1 screw and BMP.	LAE	Favorable	No	1,5
4	Canine	Siberian Husky	6 years	CF	21	Palmar fibrocartilague fx. Carpal arthrodesis	Hybrid arthrodesis plate and BMP.	RAE	Favorable	Yes[3,4]	3,5
5	Feline	European Shorthair	1 year	CF	2,8	Humerus + left femoral neck fx	Tie-in, 2 cerclages, 1 screw and BMP.	RAE	Favorable	Yes[3]	1
6	Feline	European Shorthair	1 year	M	4	P/O bone sequestrum on tibia	Bone curettage and BMP.	LPE	Favorable	Yes[4]	2
7	Canine	Mixed breed	7 years	F	6,6	Bilateral femur fx	Osteosynthesis plate, 9 screws and BMP.	RPE	Favorable	No	3
8	Canine	Yorkshire Terrier	1 year	M	3,4	Not union of radius	Synthetic Robocasted graft and BMP.	LAE	Favorable	Yes[5.1]	3
9	Canine	Bullmastiff	3 years	M	51,2	Palmar fibrocartilague fx. Carpal arthrodesis	Braun Orthomed double metacarpal plate and BMP.	RAE	Favorable	Yes[6]	4
10	Feline	European Shorthair	13 years	CM	4	Humerus fx	Intramedullary nail, 2 screws, 1 cerclage and BMP.	LAE	Slow	Yes[7]	4
11	Canine	Pointer	6 years	M	27,5	Revision of tibia fx. Leish +	DCP plate, 8 screws, cancellous bone and BMP.	LPE	Slow	Yes[7]	5
12	Canine	Labrador Retriever	8 years	M	26,8	Revision of arthrodesis. Leish +	External fixator, 2 Kirschner needles and BMP.	RAE	Slow	Yes[4,7,8,9]	10,5
13	Canine	German Shepherd	9 months	F	24,5	Femoral fx revision.	**1.** Locked nail, 4 screws and BMP/ **2.**Modified external fixator, 2 screws and BMP.	LPE	Unfavorable	Yes[3,4,5.2,8]	-

F- Female; M - Male; CF- Castrated Female; CM- Castrated Male; Fx- fracture; RAE- Right anterior extremity; LAE- Left anterior extremity; RPE- Right posterior extremity; LPE- Left posterior estremity; 1- Pain; 2- Muscular Atrophy; 3- No limb support; 4- Initial non-union; 5- Ankylosis (5.1- Carpal; 5.2- Knee); 6- Pacing, head tilt, lameness; 7- Slow consolidation; 8- Implant migration; 9- Osteolysis.

RESULTS

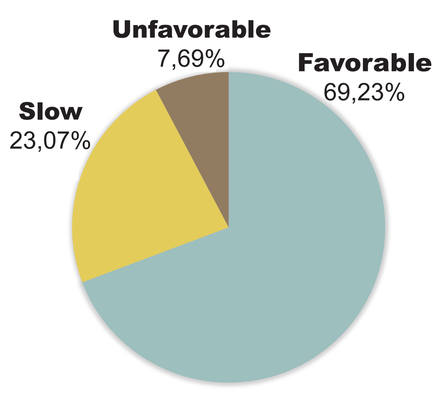

Figure 1. *Evolution of bone healing* detail in **Table 1.**

The criterion to assess the evolution of the study cases was the time of consolidation, based on the time of radiographic union. The results concerning to the evolution of bone formation are shown in **Figure 1**. We can see as an example, the **Figure 2**, that shows the evolution of case 2.

The mean time of consolidation of the 13 cases was 3.41 months and the success rate was 92.31%, considering only 1 of the cases as failure. In addition, a 76.92% of the animals showed a series of postoperative complications, that can be seen in

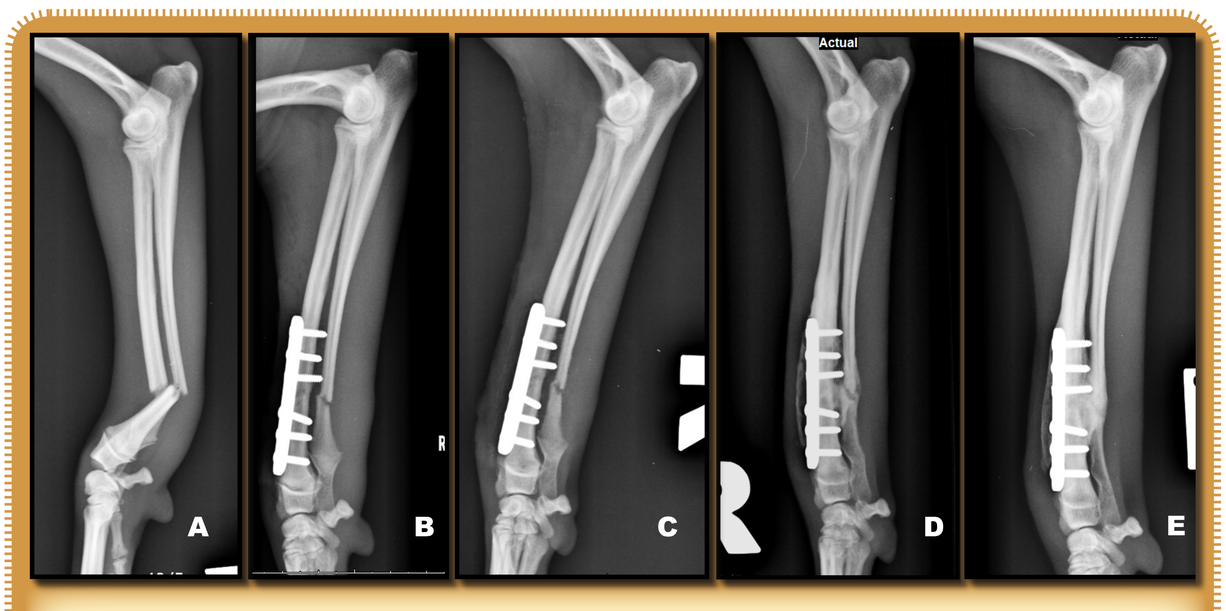

Figure 2. *Example of evolution after rhBMP-2 addition (case 2).* **A.** *Pre-operative radiography of a right ulna/radius fracture.* **B.** *Radiography 0 days post-operative.* **C.** *Radiography 7 days post-operative.* **D.** *Radiography 30 days post-operative.* **E.** *Radiography 50 days post-operative.*

DISCUSSION

In most of the study cases, the use of rhBMP resulted in an early bone healing. The results obtained were similar to those of other studies such as the one carried out by Faria et al. (2007) with open tibial fractures.

The effect of rhBMP-2 depends on the vehicle used, the amount, the concentration and the time of application, as well as the presence of enough mesenchymal cells capable of responding to BMP.

Most of the cases had no complications, or were minor. Lameness and mild inflammation are common in the first 3 weeks after implantation, but severe effects such as an excessive bone formation or the stimulation of malignant tumors are rare.

It has been seen in several studies and in the case 6, that even with osteomyelitis, the BMP remains efficient. However, diseases such as Leishmania could mask their effects by slowing down the bone formation, as happened in cases 11 and 12.

The main limitations of the study were the lack of a common criterion of choice of the cases, apart from the severity of their injuries, as well as the lack of a control group with which to compare results.

CONCLUSION

Despite its recent withdrawal from the market for commercial reasons, rhBMP-2 has been shown to be a very potent and effective osteoinductive factor in animals with delayed bone formation or non-union processes, in which its application reduces the time of radiographic union.

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